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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,241	08/05/2003	Zhen Zhang	58369 (71699)	6657
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EXAMINER DEJONG, ERIC S				
ART UNIT 1631		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/635,241

Applicant(s)

ZHANG ET AL.

Examiner

ERIC S. DEJONG

Art Unit

1631

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07/16/2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) See Continuation Sheet is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/888)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Continuation of Disposition of Claims: Claims pending in the application are 112-118,120,123,124,127,131-134,137-139,141-145,147-153,157,158,161,165-168,171-173,175-178,180-190,192,196,197,200,204,205,210-212,214-217 and 219-226.

Continuation of Disposition of Claims: Claims rejected are 112-118,120,123,124,127,131-134,137-139,141-145,147-153,157,158,161,165-168,171-173,175-178,180-190,192,196,197,200,204,205,210-212,214-217 and 219-226.

DETAILED OFFICE ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions filed on 01/22/2008 07/16/2009 has been entered.

Claims 1-111, 119, 121, 122, 125, 126, 128-130, 135, 136, 140, 146, 154-160, 162-164, 169, 170, 174, 179, 191, 193-195, 198, 199, 201-203, 206-209, 213, and 218 are canceled. Claims 225 and 226 are newly presented. Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157, 158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212, 214-217, and 219-226 are pending and currently under examination.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 149-153, 157, 158, 161, 165-168, 171-173, 176-178, 180, and 181 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. It is noted that applicants amendments are sufficient to overcome the basis of the previous rejection wherein the claims read on a computer program, per se. However, applicants amendments are not sufficient to overcome the remaining grounds of rejection, reiterated below. Further, the rejection of claims 225 and 226 are necessitated by applicants amendment to the instant claims.

Claim 149 recites the limitation "A computer readable program product embodied in a written electronic, magnetic or optical media comprising" in lines 1 and 2 of said claim. The scope of "electronic, magnetic, or optical media" as recited in the instant claim broadly encompasses signal and carrier wave embodiments of media capable of having a computer program embodied thereon. It is reiterated and emphasized that the instant claims still encompass embodiments wherein the electronic and magnetic media encompass signal and carrier wave embodiments that are also not statutory subject matter. See *In re Nuijten* (2007). Claims 150-153, 157, 158, 161, 165-168, 171-173, 176-178, 180, 181, 225, and 226 which depend from claim 149, are also included under this rejection.

Response to Arguments

Applicant's arguments filed 07/16/2009 have been fully considered but they are not persuasive because they do not address the specific basis of the rejection reiterated above, namely that the instant claims still encompass transitory signal and carrier wave embodiments that are not statutory subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 147, 148, and 221-226 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin (*The Lancet*, 359:572-577 (February 16, 2002)) in view of Golub (*Science*, 286:531-537 (Oct.

15, 1999)). The rejection of claims 225 and 226 are necessitated by applicants amendments to the instant claims.

Petricoin discloses analyzing two biological state classes – “unaffected” and “affected” wherein the affected group is known to have cancer. Petricoin discloses analyzing two independent sets of samples. Specifically, one “sample” is composed of 50 control samples for preliminary analysis, other 17 control samples, and samples from cancer patients for preliminary analysis (see p. 572-573, *Methods and Study Population*; table 1; fig. 1, p. 575, and p. 576). Thus, the analysis of the original test data is analysis of “the first set” of samples. A second “sample set” is composed of 50 control samples for the masked analysis, other unaffected samples, and benign disease control samples (p. 573-573; fig. 1, p. 575, and p. 576). Petricoin teaches that results from the test (masked data) may be added to the model/dataset to improve prediction (p. 576, right col., third full paragraph). Therefore, Petricoin discloses that both “samples” were collected and separately statistically analyzed to classify samples into different biological states (e.g., cancer and unaffected states) (fig. 1, p. 575, table 2, p. 576, left col.) AND also discloses an “intersection” subset (the totality of the data used for classification after “improvement”). Also, the results obtained from two independent samples (preliminary and masked) were “intersected” wherein data elements (key values for classifying samples, e.g., M/Z) in the intersection subset is a member of both subsets (preliminary and masked samples) (p. 576). Petricoin teaches selecting a first subset of data elements from the first data (key M/Z values) (fig. 1 and p. 575 and 576). Petricoin further discloses a preanalytical variable, e.g., medical status, a clinical

characteristic, medical condition (*e.g.*, premenopausal, menopause, age, benign diseases, *etc.*) and age distribution (*see* table 1, p. 573, p. 576). Petricoin discloses samples collected at different locations (*e.g.*, 100 control samples were provided from NOCHDP clinic in Chicago, IL, and 17 other control samples were provided by the Simone Protective Cancer Institute in Lawrenceville, NJ, p. 572-573). Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds an additional step to the method (p. 575, left col.). Petricoin discloses reshuffling (resampling) of the two highest rated sets to form new subset candidates (p. 575). Petricoin discloses selecting candidate biomarker (CA125) and testing it on a validation data set (masked serum samples, p. 575 and p. 577). Petricoin discloses a biological state is a characteristic of presence of a disease (cancer) and a biomarker is a diagnostic of a disease (CA125). Petricoin teaches that values of data elements represent level of components (proteins, p. 572, right col.) in a data point sample (M/Z values determined by MS, p. 573; *see also* peaks on fig. 2). Expression of a low-molecular-weight protein (a cancer antigen CA125) is measured by coupling serum samples with a C16 hydrophobic interaction protein chip array (an immobilized capture affinity array) and the amount of the protein is measured by SELDI-TOF mass spectrometry (p. 573, right col.). The sample of Petricoin is serum and data collected from serum relate to the cellular localization of components in a sample (*e.g.*, components located in a soluble cell fraction or "attached" to suspended cell membranes) (p. 573, left col.). Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds an additional step to the method (p.

575, left col.). Petricoin also discloses "pattern-recognition" (p. 576, right col., third full paragraph, line 10). Petricoin discloses a "classification" as a pattern recognition process (fig. 1; p. 575, left col.).

Petricoin does not expressly teach selecting a second subset and displaying the intersection subset.

Golub discloses a method for classifying cancer by using gene expression monitoring (p. 531). Golub discloses using two classes (ALL and AML acute leukemia) and two samples comprising both classes (38 initial leukemia samples and independently collected 34 leukemia samples) (p. 532, 534). Golub discloses selecting "predictors" from the first sample (38 samples) and testing the predictors on an independent 34 leukemia samples (p. 532). Golub further discloses prediction strengths for both the initial (cross-validation) sample and an independent sample and selection of data elements with high prediction strength for both samples (selecting a first and a second subset) (p. 543 and fig. 3). Golub also discloses comparing two samples wherein the structure (data elements – gene predictors) in the initial sample is also seen in the independent sample (*i.e.*, samples are intersected) (p. 534, middle col. and fig. 4). Golub discloses displaying the intersection (fig. 3). Golub discloses that different types of samples, bone marrow and blood, were collected by different protocols (*e.g.*, samples from SJCRH were processed with a very different protocol) (p. 536-537, paragraph 23). Also, collection of bone marrow and blood requires different protocols. Golub discloses collecting samples at different collecting sites and from different populations (p. 536-537, paragraph 23).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin to select both a first and a second subset of data elements and display the intersection, as taught by Golub, where the motivation would have been to test a model/hypothesis and to compare results from a model and a test, as taught by Golub, p. 534.

Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157, 158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212, 214-217, and 219-226 are rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin (*The Lancet*, 359:572-577 (February 16, 2002)) in view of Golub (*Science*, 286:531-537 (Oct. 15, 1999)), as applied to claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 147, 148, and 221-224 above, and in further view of Barnhill (U.S. Patent 6,789,069).

Petricoin and Golub make obvious claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 148, and 221-224, as set forth above.

Petricoin also discloses using mass spectrometry (*i.e.*, SELDI) for acquiring and processing experimental data and bioinformatics software for processing data (p. 573 and 575). Petricoin discloses a computer based chip system (the Protein Biology System 2 SELDI-TOF mass spectrometer such as CIPHERGEN Biosystems with a detector and a chip reader, p. 573). Petricoin also discloses that data were collected and were used later for analysis (*i.e.*, data are stored).

Petricoin and Golub do not disclose a supervised learning algorithm and specifically, a support vector machine analysis; protein binding partners in an expression profiling assay; and a computer system and a computer readable medium for performing the method.

Barnhill discloses a method for classifying unknown samples using a learning machine, similar to that of Petricoin. Barnhill discloses different methods for data acquisition such as nucleic acid arrays and protein expression assays (e.g., antibody chips to identify specific proteins, col. 13, line 5-15). Barnhill method comprises acquiring expression data and processing data via creating training set by using a support vector machine and using the set to classify unknown data (col. 5, line 1-54). Barnhill discloses a gene chip, a mass spectrometer, and a protein binding assay comprising a protein binding partner (col. 1-2 and col. 13, line 5-15).

Barnhill discloses a computer system and a program for executing his method wherein data are entered into a computer system via a user interface (col. 22, line 27-67 and fig. 10-12), qualified, and selected (see for a general description of a computer system and programs col. 21, line 27 – col. 26, line 38 and fig. 10-12). The system comprises a processor, an input device, a memory, programs, and a network connector (fig. 10). Example 1 illustrates the method and the system for executing the method of Barnhill wherein tables 2-4 represent a database of ranked data obtained during the execution of the method (col. 38-42).

It would have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a supervised learning algorithm and

specifically, a support vector machine analysis, as taught by Barnhill, where the motivation would have been to improve pre-and post-processing data and maximize the value of genomic and proteomic information, as taught by Barnhill, col. 4, line 29-33. It would further have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a protein expression assay, as taught by Barnhill, where the motivation would have been to determine efficiently specific proteins from a large protein expression pool, as taught by Barnhill (col. 12, line 10 – col. 13, line 15). It would have also been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a computer and a computer readable medium for executing Petricoin's method, as taught by Barnhill, where the motivation would have been to manage large amount of complicated data in genomic and proteomic investigations, as taught by Barnhill, col. 1-2.

Response to Arguments

Applicant's arguments filed 07/16/2009 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and in further view of Barnhill, applicants reiterate previously presented grounds of argument that Petricoin does not teach the selection of subsets from the first and second data sets nor does Petricoin teach or suggest the selection of an intersection subset from these subsets. Applicants further argue that Petricoin nor

any other cited documents (i.e. Golub and Barnhill) disclose or suggest the step of selecting an intersection subset of data elements as recited in claim 112, a third computer readable program providing instructions for selection an intersection subset of data elements, as recited in claim 149, executing computer readable program code for selecting an intersection subset of data elements as recited in claim 182.

In response, it is noted that applicants reiterate previous presented arguments directed toward the prior art of record in comparison to ***the exact terms recited in the instant claims***. As such, applicants arguments are not persuasive for reasons already of record. It is emphasized that the recent Supreme Court decision in KSR Intl. Co. v. Teleflex Inc. rejected the rigid approach of applying a strict TSM test as the sole basis for obviousness and that the analysis ***for obviousness need not seek out precise teachings directed to the specific subject matter of a claim***. Further the decision set forth that ***the analysis can take into account the inferences and creative steps that a person of ordinary skill in the art could employ and that a person of ordinary skill in the art is also a person of ordinary creativity***, not an automaton. Further, the decision set forth that a combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.

Applicants reiterated arguments only serve to emphasize where the precise language of the instant claims is not found in the prior art relied upon in the instant rejection. It is emphasized that the instant rejection is not based upon a finding of exact anticipation as would be required under 35 USC § 102, but is rather based upon a finding of obviousness under 35 USC 103(a). The examiner acknowledges that, as set

forth in the rejection above, there are differences between the precise teachings of the art and the precise limitations recited in the instant claims. However, upon full consideration and review of the art of record, these differences all appear to be well within the scope of the skill set attributed to an artisan in this field. Applicants reiterated arguments do not establish how the precise language of the instant claims rise above a mere more combination of familiar elements which yield predictable results as seen through the eyes of one of skill in this art. Therefore, applicants argument remains unpersuasive.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERIC S. DEJONG whose telephone number is (571)272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ERIC S. DEJONG/
Primary Examiner, Art Unit 1631